CLINICAL AUDIT

Distal adenomatous polyps are rare in patients with inflammatory bowel disease

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Objective: There is an increased risk of colorectal cancer in patients with inflammatory bowel disease (IBD). The aim of this study was to compare the prevalence of left sided adenomas in patients with IBD aged 55–64 years with a local age matched control population.

Method: A review of clinical notes. The prevalence of adenomas in patients with IBD attending for either sigmoidoscopy or colonoscopy was compared with local age matched controls that participated in the national screening trial for colorectal cancer with flexible sigmoidoscopy.

Results: Of 106 patients (61 male, 45 female, mean age of 59 years), 80 suffered from ulcerative colitis, 20 from Crohn's disease, and six from indeterminate colitis. All patients had undergone at least one flexible sigmoidoscopy and 75 had a colonoscopy. Distal adenomas were found in three patients with ulcerative colitis compared with 67 of 749 controls (2.8% *v* 8.9%, $\chi^2 = 4.6$, $p = 0.03$).

Conclusions: The results suggest that distal adenomatous polyps are rare in patients aged 55–64 years with IBD compared with a control population. This supports the hypothesis that lesions other than polyps are important for the development of colorectal cancer in patients with IBD.

The risk of colorectal cancer in inflammatory bowel disease (IBD) is significantly increased when compared with the normal population.[1–3] The risk of developing colorectal cancer in longstanding ulcerative colitis (UC) and Crohn's disease (CD) is 5%–13%. It is common practice that both of these conditions undergo regular surveillance colonoscopy.[4] The risk factors for developing colorectal cancer in IBD seem to be duration of disease, extent of the disease, early age of diagnosis, complicating factors such as sclerosing cholangitis, and persistent disease activity.[5 6] Colorectal cancer in IBD patients may occur throughout the entire length of the colon or may be multi-focal. Similar to sporadic tumours, most occur in the left colon. The proportion of Dukes's staging A to C of IBD related colorectal cancer is similar to that of sporadic cancers seen in the general population. The prognosis and overall survival is also similar at 40% at five years.[7] The mechanism of colorectal cancer in IBD is yet to be established, but development of non-polypoid dysplasia seems to be the most important predictive factor of an underlying malignancy and potential for malignant transformation. In sporadic colorectal cancer, the adenoma-carcinoma sequence is well established.[8] Polyps with epithelial dysplasia in UC represent either dysplasia associated lesions or masses (DALMs) or sporadic adenomas. DALMs are commonly associated with carcinoma and are an indication for colectomy.[9] However, if the adenomatous DALM lesion is removed and the surrounding mucosa has no evidence of flat dysplasia then it can be surveyed intensively. Removal of the polyp is the treatment of choice for sporadic adenomas.[10–12] 5-ASA compounds are prescribed as a maintenance therapy to reduce the risk of relapse in patients with IBD and recent reports suggest they may also protect against colorectal cancer although the mechanism of action is not known.[13–15]

The aim of this retrospective study was to compare the prevalence of simple adenomatous polyp lesions in IBD patients with an age matched healthy population.

METHODS

Patients aged 55–64 years with IBD undergoing sigmoidoscopy or colonoscopy between 1995 and 2002 inclusive were identified from computed endoscopy and histopathology databases within the University Hospitals Leicester NHS Trust. Patients with histologically confirmed UC, indeterminate or colonic CD were included. The medical records were then reviewed to establish disease type, extent, procedure type, and the patient use of 5-ASA or immunosuppressant plus the identification of adenomatous polyps.

Where patients had more than one endoscopic examination during the ages of 55–64, the last endoscopy only was included in the analysis, but all past procedures were also evaluated to ensure adenomatous polyps had not been removed from the patient in the past. Operators were mixed (consultant and specialist registrar) in the IBD group and consultant led in the screening group. The frequency of polyps was compared with that of a control group of 749 healthy volunteers aged 55–64 years who participated within the Leicestershire arm of the national screening trial for the prevention of colorectal cancer using flexible sigmoidoscopy during 1995–1997.[16 17] The volunteers had no history of bowel conditions, previous investigations, or significant family history.

The frequency of polyps between patients with IBD and controls was compared by use of the χ^2 test.

RESULTS

One hundred and six patients had a histological diagnosis of IBD at either sigmoidoscopy or colonoscopy. Of these patients 61 (57.5%) were male and 45 (42.5%) were female and the mean age was 59. Eighty patients (75.5%) had a diagnosis of UC, 20 patients (18.9%) had CD, and six patients (5.6%) had indeterminate colitis. Colonoscopy was performed in 75 (70.7%) patients and flexible sigmoidoscopy in the remaining 31 (29.2%) patients. Twenty six (24.5%) of the patients were diagnosed with IBD at the time of endoscopy in question. The average disease duration for the remaining 80 (73.5%) patients was 13.28 years (range 1 to 41 years). Differences in procedures undertaken were attributable to choice, reasons included sigmoidoscopy being used as first line investigation

Abbreviations: IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; DALM, dysplasia associated lesion or masse

Table 1 Disease extent in patients with inflammatory bowel disease

Extent of disease	Number of patients
Pancolitis	55
Left sided	23
Recto/sigmoid	24
Patchy	2
Right sided	2

or to assess those with symptoms unresponsive to therapy and colonoscopy for surveillance purposes.

Extent of disease was determined by histological examination in those undertaking colonoscopy and in those with sigmoidoscopy extent was taken as far as the observations were made. Fifty five (51.8%) patients had pancolitis, 23 (21.6%) had left sided disease, and 24 (22.6%) patients had disease limited to the rectosigmoid area. Patchy disease was seen in two (1.8%) patients and disease limited to the right side was also seen in two (1.8%) patients (table 1).

No patients in the IBD group had evidence of colorectal cancer. Dysplasia was seen in six (5.6%) patients, five of whom had low grade dysplasia (including the patients with polyps). One patient was labelled as having ''moderate'' dysplasia not fitting standard dysplasia definition.

Only three (2.8%) patients with IBD were found to have adenomatous polyps all associated with low grade dysplasia (table 2).

Of the three patients, one (male) patient had a 15 year history of pan-UC and a 8 mm rectal tubular adenoma with low grade dysplasia. The second (female) patient had a four year history of ulcerative proctitis and was found to have a 2 mm rectal adenoma, which showed low grade dysplasia. The third (male) patient with UC was found at the time of diagnosis to have a 20 mm tubulovillous adenoma at 20 cm distance, with low grade dysplasia. The third patient was at a later endoscopy shown to have pancolitis. All three of the patients with adenomatous polyps had their polyp identified at sigmoidoscopy and within the affected part of bowel. Both patients with longstanding IBD had been using a 5-ASA product since the time of diagnosis. The other was given 5-ASA at the time of diagnosis. Four (3.77%) of the patients had a family history of colorectal cancer one of whom was found to have adenomatous polyp (the second patient). Pseudo-polyps were found in six (5.66%) patients, none of which were present in conjunction with adenomatous polyps. Two (1.88%) patients where found to have metaplastic polyps. In the asymptomatic healthy control population, adenomatous polyps were found in 67 of 749 patients (8.9%), compared with the 2.8% found in the IBD group ($\chi^2 = 4.6$, $p = 0.03$). There is no distinction in the records of these patients between spontaneous adenoma and DALMs lesion and the patients were managed as for non-IBD adenomas—that is, with the removal of the polyp rather than colectomy.

Table 2 Presence of adenomatous polyps in inflammatory and control groups

	Adenomatous polyps present	Number of patients
Control	67 (8.9%)	749
IBD patients	3 (2.8%)	106
	2.8% *v* 8.9%, $\chi^2 = 4.6$, $p = 0.03$	

Table 3 Use of 5-ASA compounds and azathioprine

Drug name	Number of patients
Asacol	21
Mesalazine	25
Salazopyrine	17
Pentasa	5
Olsalazine	1
Balsalazide	1
Intolerance to 5-ASA	4
No drug therapy	24
Azathioprine	6
Previous azathioprine trial	2

Seventy five patients (70.7%) at the time of endoscopy were taking 5-ASA compounds. Thirty (28.3%) patients in the IBD group were shown to have been prescribed a 5-ASA compound started at the time of diagnosis/presentation. Azathioprine use was less common with only six (5.6%) of patients using it at the time of endoscopy. Table 3 shows the break down of 5-ASA use and azathioprine. Mesalazine is stated when no specific brand is named in the records.

Some of the group had undergone one or more operative procedures but none of whom had had previous adenomatous polyp removal. In the patients with CD, two had had small bowel resections, one right hemicolectomy and an ileoceacal resection with stricture resection. One patient had undergone a left hemicolectomy. It was noted that after the endoscopic process reportted in the study, six (5.6%) patients subsequently went on to have total colectomies, which occurred as a sequelea to a flare up, and four (3.7%) patients went on to have subtotal colectomies associated with flare up. No operative specimens of the patients showed adenomatous polyps or dysplasia at histological examination.

DISCUSSION

Results of this study suggest that adenomatous polyps are rare in patients with IBD. These findings support the hypothesis that mechanisms other than the adenoma-carcinoma sequence are important in the development of colorectal carcinoma in IBD. These data support the hypothesis that the non-adenomatous dysplasia-carcinoma sequence seems to be more important in patients with IBD than the adenoma-carcinoma sequence.[18] The reasons why adenomatous polyps are uncommon in IBD is unclear, but the possible protective role of 5-ASA preparations is intriguing. 5-ASA drugs may protect against colorectal cancer in IBD,[1] but their mechanisms of action are unknown. In patients with adenomas, 5-ASA drugs have been shown to reduce adenoma size and also possibly prevent adenoma formation.[13] It is therefore possible that 5-ASA preparations act in IBD by preventing adenoma formation. This itself is an area requiring further investigation with adequately powered prospective studies.

This study has several limitations in that it is retrospective, hospital based, and bias within the study group may have been introduced by a mixture of baseline (new diagnosis) and surveillance procedures. There is no distinction from the data between the lesions being possibly an IBD related dysplastic lesion or a sporadic adenoma. Polyps within areas of inflamed tissue may be harder to detect and therefore may be missed, also small polyps may be missed when combined with pseudo polyps. Certainly in our group there is a low rate of inflammatory polyps recorded and to this end adenomatous polyps may also be under reported. Senior staff only undertook endoscopies in the control group, but in the IBD group there was a mixture of registrars and consultants undertaking endoscopy. The indication for the chosen

investigation also differs between the screening group and the IBD group. In IBD patients the intent of the investigation is to assess the extent and activity of the disease and there is less emphasis on polyp detection compared with the screening group giving rise to detection bias. It could be argued that patients undergoing surveillance are more health conscious and more likely to be taking long term 5-ASA preparations, so decreasing the chance of polyp formation. Paradoxically, the two patients with longstanding IBD with adenomatous polyps found at endoscopy were both taking 5-ASA compounds. The polyp prevalence for the whole flexible sigmoidoscopy trial was 12.9% giving a higher prevalence than the small local cohort used in this study. This study does not take into account matching of smoking and any family history in the two groups.

Recent work published by Kitiyakara[19] also looked at the prevalence of dysplastic polyps in patients with UC and compared them with patients undergoing colonoscopy for changed bowel habit. They also concluded that there is a low prevalence of adenomatous polyps in patients with IBD compared with local age matched controls. They also took the study further by looking at the classification of these lesions in terms of dysplasia and DALMS and discuss the management differences between the lesions. Our work adds to the growing amount of data showing decreased prevalence of adenomatous polyps in patients with IBD and strengthens the debate on potential mechanisms involved in IBD cancer formation.

Future work should involve prospective studies of IBD patients and controls, which accurately measure adenomatous polyp formation rate, which as yet is unknown. 5-ASA compounds may be responsible for a decreased formation of adenomatous polyps in patients with IBD. This intriguing role could see the use of 5-ASA compounds widened to patients at risk of colorectal cancers such as non-IBD patients with adenomatous polyps or those with a strong family history. Further evaluation is needed in this area.

In summary, this retrospective study showed that distal adenomatous polyps are rare in patients with IBD (despite a higher risk of colorectal cancer) suggesting a different mechanism of tumour formation may be involved. These findings need to be confirmed in large prospective studies and further work is needed in the mechanisms involved.

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REFERENCES

1 **Eaden JA**, Abrams KR, Ekbom A, *et al*. Colorectal cancer prevention in ulcerative colitis: a case control study. *Aliment Pharmacol Ther* 2000;**14**:145–53.
2 **Pohl C**, Hombach A, Kruis W. Chronic inflammatory bowel disease and cancer. *Hepatogastroenterology* 2000;**47**:57–70.
3 **Persson PG**, Karlen P, Bernell O, *et al*. Crohn's disease and cancer: a population-based cohort study. *Gastroenterology* 1994;**107**:1675–9.
4 **Fefferman DS**, Farrell RJ. Endoscopy in inflammatory bowel disease: indications, surveillance, and use in clinical practice. *Clin Gastroenterol Hepatol* Jan, 2005;**3**:11–24.
5 **Pinczowski D**, Ekbom A, Baron J, *et al*. Risk factors for colorectal cancer in patients with ulcerative colitis:a case controlled study. *Gastroenterology* 1994;**107**:117–20.
6 **Munkholm P**, Langholz E, Davidson M, *et al*. Intestinal cancer risk and mortality in patients with Crohn's disease. *Gastroenterology* 1993;**105**:1716–72.
7 **Wolmark N**, Fisher B, Wiend H. The prognostic value of the modification of the Dukes' C class of colorectal cancer. *Ann Surg* 1986;**203**:115.
8 **Vogelstein B**, Kinzler K. *The genetic basis of human cancer*. New York: McGraw-Hill, 1998:565–87.
9 **Rubin P**. Adenoma in ulcerative colitis, endoscopic polypectomy or colectomy. *Inflamm Bowel Dis* 1999;**30**:898–905.
10 **Petras RE**. The significance of ''adenomas'' in ulcerative colitis: deciding when a colectomy should be performed. *Inflamm Bowel Dis* 1999;**5**:306–8.
11 **Fogt F**, Urbanski SJ, Sanders ME, *et al*. Distinction between dysplasia-associated lesion or mass (DALM) and adenoma in patients with ulcerative colitis. *Hum Pathol* 2000;**31**:288–91.
12 **Engelsgjerd M**, Farraye FA, Odze RD. Polypectomy may be adequate treatment of adenoma-like dysplastic lesions in chronic ulcerative colitis. *Gastroenterology* 1999;**117**:1288–94.
13 **Eaden J**. Review article: the data supporting a role for aminosalicylates in the chemoprevention of colorectal cancer in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2003;**18**(suppl 2):15–21.
14 **Moody GA**, Jayanthi V, Probert CS, *et al*. Long term therapy with sulphasalazine protects against colorectal cancer in ulcerative colitis: a retrospective study of colorectal cancer and compliance with treatment in Leicestershire. *Eur J Gastroenterol Hepatol* 1996;**8**:1179–83.
15 **Eaden JA**, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta analysis. *Gut* 2001;**48**:526–35.
16 **Hart AR**, Wicks AC, Mayberry JF. Colorectal cancer screening in asymptomatic populations. *Gut* 1995;**36**:590–8.
17 **Hart AR**, Kudo S, Mackay EH, *et al*. Flat adenomas exist in asymptomatic people: important implications for colorectal cancer screening programmes. *Gut* 1998;**43**:229–31.
18 **Collins RH Jr**, Feldman M, Fordtran JS. Colon cancer, dysplasia and surveillance in patients with ulcerative colitis. A critical review. *N Engl J Med* 1987;**316**:1654.
19 **Kitiyakara T**, Bailey DM, McIntyre AS, *et al*. Adenomatous colonic polyps are rare in ulcerative colitis. *Aliment Pharmacol Ther* 2004;**19**:879–87.